

GCTATAAGGA TCACGGCGCCC CAGTCGACGC TGAGCTCCTC TGCTACTCAG AGTTGCAACC TCAGCCTCGCT
 ATG GCT CCC AGC AGC CCC CGG CCC CTG GCG CTG CTC CTG GTC CTC GGT GGT CTG TTC CCA
 MET ALA PRO SER SER PRO ARG PRO ALA LEU PRO ALA LEU LEU VAL LEU LEU GLY ALA LEU PHE PRO
 GGA CCT GGC AAT GCC CAG ACA TCT GTG TCC CCC TCA AAA GTC ATC CTG CCC CGG GGA GGC TCC GTG
 GLY PRO GLY ASN ALA GLN THR SER VAL SER PRO SER LYS VAL ILE LEU PRO ARG GLY SER VAL
 CTG GTG ACA TGC AGC ACC TCC TGT GAC CAG CCC AAG TTG TCG GGC ATA GAG ACC CCG TTG CCT AAA
 LEU VAL THR CYS SER THR SER CYS ASP GLN PRO LYS LEU LEU GLY ILE GLU THR PRO LEU PRO LYS
 AAG GAG TTG CTC CTG CCT GGG AAC AAC CGG AAG GTG TAT GAA CTG AGC AAT GTG CAA GAA GAT AGC
 LYS GLU LEU LEU LEU PRO GLY ASN ASN ARG LYS VAL TYR GLU LEU SER ASN VAL GLN GLU ASP SER
 CAA CCA ATG TGC TAT TCA AAC TGC CCT GAT GGG CAG TCA ACA GCT AAA ACC TTC CTC ACC GTG TAC
 GLN PRO MET CYS TYR SER ASN CYS PRO ASP GLY GLN SER THR ALA LYS THR PHE LEU THR VAL TYR
 TGG ACT CCA GAA CGG GTG GAA CTG GCA CCC CTC CCC TCT TGG CAG CCA GTG GGC AAG AAC CTT ACC
 TRP THR PRO GLU ARG VAL GLU LEU ALA PRO LEU PRO SER TRP GLN PRO VAL GLY LYS ASN LEU THR
 CTA CGC TGC CAG GTG GAG GGT GGG GCA CCC CGG GCC AAC CTC ACC GTG GTG CTC CTG GGT GAG
 LEU ARG CYS GLN VAL GLU GLY GLY ALA PRO ARG ALA ASN LEU THR VAL LEU ARG GLY GLU
 AAG GAG CTG AAA CGG GAG CCA GCT GTG GGG GAG CCC GCT GAG GTC ACC AGC GTG CTG GTG AGG
 LYS GLU LEU LYS ARG GLU PRO ALA VAL GLY GLU PRO ALA GLU VAL THR THR THR VAL LEU VAL ARG
 AGA GAT CAC CAT GGA GCC AAT TTC TCG TGC CGC ACT GAA CTG GAC CTG CGG CCC CAA GGG CTG GAG
 ARG ASP HIS HIS GLY ALA ASN PHE SER CYS ARG THR GLU LEU ASP LEU ARG PRO GLN GLY LEU GLU

FIG. 1A

CTG TTT GAG AAC ACC TCG GCC CCC TAC CAG CTC CAG ACC TTT GTC CTG CCA GCG ACT CCC CCA CAA	LEU PHE GLU ASN THR SER ALA PRO TYR GLN LEU GLN THR PHE VAL LEU PRO ALA THR PRO PRO GLN
CTT GTC AGC CCC CGG GTC CTA GAG GTG GAC ACG CAG GGG ACC GTG GTC TGT TCC CTG GAC GGG CTG	LEU VAL SER PRO ARG VAL LEU GLU VAL ASP THR GLN GLY THR VAL VAL CYS SER LEU ASP GLY LEU
TTT CCA GTC TCG GAG GCC CAG GTC CAC CTG GCA CTG GGG GAC CAG AGG TTG AAC CCC ACA GTC ACC	PHE PRO VAL SER GLU ALA GLN VAL HIS LEU ALA LEU GLY ASP GLN ARG LEU ASN PRO THR VAL THR
TAT GGC AAC GAC TCC TTC TCG GCC AAG GCC TCA GTC AGT GTG ACC GCA GAG GAC GAG GGC ACC CAG	TYR GLY ASN ASP SER PHE SER ALA LYS ALA SER VAL SER VAL THR ALA GLU ASP GLU GLY THR GLN
CGG CTG ACG TGT GCA GTA ATA CTG GGG AAC CAG AGC CAG GAG ACA CTG CAG ACA GTG ACC ATC TAC	ARG LEU THR CYS ALA VAL ILE LEU GLY ASN GLN SER GLN GLU THR LEU GLN THR VAL THR ILE TYR
AGC TTT CCG GCG CCC AAC GTG ATT CTG ACG AAG CCA GAG GTC TCA GAA GGG ACC GAG GTG ACA GTG	SER PHE PRO ALA PRO ASN VAL ILE LEU THR LYS PRO GLU VAL SER GLU GLY THR GLU VAL THR VAL
AAG TGT GAG GCC CAC CCT AGA GCC AAG GTG ACG CTG AAT GGG GTT CCA GCC CAG CCA CTG GGC CCG	LYS CYS GLU ALA HIS PRO ARG ALA LYS VAL THR LEU ASN GLY VAL PRO ALA GLN PRO LEU GLY PRO
AGG GCC CAG CTC CTG AAG GCC ACC CCA GAG GAC AAC GGG CGC AGC TTC TCC TGC TCT GCA ACC	ARG ALA GLN LEU LEU LEU LYS ALA THR PRO GLU ASP ASN GLY ARG SER PHE SER CYS SER ALA THR
CTG GAG GTG GCC GGC CAG CTT ATA CAC AAG AAC CAG ACC CCG GAG CTT CGT GTC CTG TAT GGC CCC	LEU GLU VAL ALA GLY GLN LEU ILE HIS CAC AAG AAC CAG ACC CCG GAG CTT CGT GTC CTG TAT GGC CCC
CGA CTG GAC GAG AGG GAT TGT CCG GGA AAC TGG ACG TGG CCA GAA AAT TCC CAG CAG ACT CCA ATG	ARG LEU ASP GLU ARG ASP CYS PRO PRO GLY ASN TRP THR TRP PRO GLU ASN SER GLN GLN THR PRO MET
TGC CAG GCT TGG GGG AAC CCA TTG CCC GAG CTC AAG TGT CTA AAG GAT GGC ACT TTC CCA CTG CCC	CYS GLN ALA TRP GLY ASN PRO LEU PRO GLU LEU LYS CYS LEU LYS ASP GLY THR PHE PRO LEU PRO

FIG. 1B

ATC GGG GAA TCA GTG ACT GTC ACT CGA GAT CTT GAG GGC ACC TAC CTC TGT CGG GCC AGG AGC ACT
 ILE GLY GLU SER VAL THR VAL THR VAL THR ARG ASP LEU GLU GLY THR TYR LEU CYS ARG ALA ARG SER THR

 CAA GGG GAG GTC ACC CGC GAG GTG ACC GTG AAT GTG CTC TCC CCC CGG TAT GAG ATT GTC ATC ATC
 GLN GLY GLU VAL THR ARG GLU VAL THR VAL ASN VAL LEU SER PRO ARG TYR GLU ILE VAL ILE ILE

 ACT GTG GTA GCA GCC GCA GTC ATA ATG GGC ACT GCA GGC CTC ACC GCG TAC CTC TAT AAC CGC CAG
 THR VAL VAL ALA ALA VAL ILE MET GLY THR ALA GLY LEU SER THR TYR LEU TYR ASN ARG GLN

 CGG AAG ATC AAG AAA TAC AGA CTA CAA CAG GCC CAA AAA GGG ACC CCC ATG AAA CCG AAC ACA CAA
 ARG LYS ILE LYS LYS TYR ARG LEU GLN GLN ALA GLN LYS GLY THR PRO MET LYS PRO ASN THR GLN

 GCC ACG CCT CCC TGA ACCTATCCCG GGACAGGGCC TCTTCCTCGG CCTTCCCATTA TTGGTGGCAG TGGTGCCACA
 ALA THR PRO PRO ***

 CTGAACAGAG TGAAGACAT ATGCCATGCA GCTACACCTA CCGGCCCTGG GACGCCGGAG GACAGGGCAT TGTCTCAGT

 CAGATACAAC AGCATTTGGG GCCATGGTAC CTGCACACCT AAAACACTAG GCCAGGCATC TGATCTGTAG TCACATGACT

 AAGCCAAAGAG GAAGGAGCAA GACTCAAGAC ATGATTGATG GATGTTAAAG TCTAGCCTGA TGAGAGGGGA AGTGGTGGG

 GAGACATAGC CCCACCATGA GGACATACAA CTGGGAAATA CTGAAACTTG CTGCCATTG GGTATGCTGA GGGCCACAGA

 CTTACAGAAG AAGTGGCCCT CCATAGACAT GTGTAGCATC AAAACACAAA GGGCCACACT TCCTGACGGA TGCCAGCTTG

 GGCAGTGTG TCTACTGACC CCAACCCCTG ATGATATGTA TTTATTCATT TGTATTATTA CCAGCTATTT ATTGAGTGT

 TTTTATGTAG GCTAAATGAA CATAGGTCTC TGGCCTCACC GAGCTCCCAG TCCATGTCAC ATTCAAGGTC ACCAGGTACA

 GTTGTACAGG TTGTACACTG CAGGAGAGTG CCTGGCAAAA AGATCAAAATG GGGCTGGGAC TTCTCATTTG CCAACCTGCC

 TTTCCCCAGA AGGAGTGATT TTTCTATCGG CACAAAAGCA CTATATGGAC TGGTAATGGT TCACAGGTTT AGAGATTACC

FIG. 1C

CAGTGAGGCC TTATTCCCTCC CTTCCCCCCA AACTGACAC CTTTGTTAGC CACCTCCCCA CCCACATACA TTTCTGCCAG
TGTTACAATG ACACTCAGCG GTCATGTCTG GACATGAGTG CCCAGGGAAT ATGCCCCAAGC TATGCCCTTGT CCTCTTGTCC
TGTTTGCATT TCACTGGGAG CTTGCCACTAT TGCAGCTCCA GTTTCCTGCA GTGATCAGGG TCCTGCAAGC AGTGGGGAAG
GGGGCCAAGG TATTGGAGGA CTCCTTCCCA GCTTTGGAAG GGTCAATCCGC GTGTGTGTGT GTGTGTATGT GTAGACAAGC
TCTCGCTCTG TCACCCAGGC TGGAGTGCAG TGGTGCAATC ATGGTCACT GCAGTCTGA CCTTTTGGGC TCAAGTGATC
CTCCACCTC AGCCTCCTGA GTAGCTGGGA CCATAGGCTC ACAACACCCAC ACCTGGCAA TTTGATTTTT TTTTTTTTTT
TCAGAGACGG GGTCTCGCAA CATTGCCCAG ACTTCCTTG TGTAGTTAA TAAAGCTTC TCAACTGCCA AAAAAAAA
AAAAAA

FIG. 1D

FIG. 2A

TTCACATCAA AACTCCTATA CTGACCTGAG ACAGAGGCAG CAGTGATACC CACCTGAGAG ATCCTGTGTT TGA
 ACAACTG CTTCCCAAAA CGGAAAGTAT TTCAAGCCTA AACCTTTGGG TGAAGAAGAAC TCTTGAAGTC ATG ATT
 met. ile
 GCT TCA CAG TTT CTC TCA GCT CTC ACT TTG GTG CTT CTC ATT AAA GAG AGT GGA GCC TGG
 ala ser gln phe leu ser ala leu thr leu val leu leu ile lys glu ser gly ala trp
 TCT TAC AAC ACC TCC ACG GAA GCT ATG ACT TAT GAT GAG GCC AGT GCT TAT TGT CAG CAA
 ser tyr asn thr ser thr glu ala met thr tyr asp glu ala ser ala tyr cys gln gln
 AGG TAC ACA CAC CTG GTT GCA ATT CAA AAC AAA GAA GAG ATT GAG TAC CTA AAC TCC ATA
 arg tyr thr his leu val ala ile gln asn lys glu glu ile glu tyr leu asn ser ile
 TTG AGC TAT TCA CCA AGT TAT TAC TGG ATT GGA ATC AGA AAA GTC AAC AAT GTG TGG GTC
 leu ser tyr ser pro ser tyr tyr trp ile gly ile arg lys val asn asn val trp val
 TGG GTA GGA ACC CAG AAA CCT CTG ACA GAA GAA GCC AAG AAC TGG GCT CCA GGT GAA CCC
 trp val gly thr gln lys pro leu thr glu glu ala lys asn trp ala pro gly glu pro
 AAC AAT AGG CAA AAA GAT GAG GAC TGC GTG GAG ATC TAC ATC AAG AGA GAA AAA GAT GTG
 asn asn arg gln lys asp glu asp cys val glu ile tyr ile lys arg glu lys asp val
 GCC ATG TGG AAT GAT GAG AGG TGC AGC AAG AAG AAG CTT GCC CTA TGC TAC ACA GCT GCC
 gly met trp asn asp glu arg cys ser lys lys leu ala leu cys tyr thr ala ala
 TGT ACC AAT ACA TCC TGC AGT GGC CAC GGT GAA TGT GTA GAG ACC ATC AAT AAT TAC ACT
 cys thr asn thr ser cys ser gly his gly glu cys val glu thr ile asn asn tyr thr
 TGC AAG TGT GAC CCT GGC TTC AGT GGA CTC AAG TGT GAG CAA ATT GTG AAC TGT ACA GCC
 cys lys cys asp pro gly phe ser gly leu lys cys glu gln ile val asn cys thr ala

CTG GAA TCC CCT GAG CAT GGA AGC CTG GTT TGC AGT CAC CCA CTG GGA AAC TTC AGC TAC
 leu glu ser pro glu his gly ser leu val cys ser his pro leu gly asn phe ser tyr
 AAT TCT TCC TGC TCT ATC AGC TGT GAT AGG GGT TAC CTG CCA AGC AGC ATG GAG ACC ATG
 asn ser ser cys ser ile ser cys asp arg gly tyr leu pro ser ser met glu thr met
 CAG TGT ATG TCC TCT TCT GGA GAA TGG AGT GCT CCT ATT CCA GCC TGC AAT GTG GTT GAG TGT
 gln cys met ser ser gly glu trp ser ala pro ile pro ala cys asn val val glu cys
 GAT GCT GTG ACA AAT CCA GCC AAT GGG TTC GTG GAA TGT TTC CAA AAC CCT GGA AGC TTC
 asp ala val thr asn pro ala asn gly phe val glu cys phe gln asn pro gly ser phe
 CCA TGG AAC ACA ACC TGT ACA TTT GAC TGT GAA GAA GGA TTT GAA CTA ATG GGA GCC CAG
 pro trp asn thr thr cys thr phe asp cys glu glu gly phe glu leu met gly ala gln
 AGC CTT CAG TGT ACC TCA TCT GGG AAT TGG GAC AAC GAG AAG CCA ACG TGT AAA GCT GTG
 ser leu gln cys thr ser ser gly asn trp asp asn glu lys pro thr cys lys ala val
 ACA TGC AGG GCC GTC CGC CAG CCT CAG AAT GGC TCT GTG AGG TGC AGC CAT TCC CCT GCT
 thr cys arg ala val arg gln pro gln asn gly ser val arg cys ser his ser pro ala
 GGA GAG TTC ACC TTC AAA TCA TCC TGC AAC TTC ACC TGT GAG GAA GGC TTC ATG TTG CAG
 gly glu phe thr phe lys ser ser cys asn phe thr cys glu glu gly phe met leu gln
 GGA CCA GCC CAG GTT GAA TGC ACC ACT CAA GGG CAG TGG ACA CAG CAA ATC CCA GTT TGT
 gly pro ala gln val glu cys thr thr gln gly gln trp thr thr gln gln ile pro val cys
 GAA GCT TTC CAG TGC ACA GCC TTG TCC AAC CCC GAG CGA GGC TAC ATG AAT TGT CTT CCT
 glu ala phe gln cys thr ala leu ser asn pro glu arg gly tyr met asn cys leu pro

FIG. 2B

AGT	GCT	TCT	GGC	AGT	TTC	CGT	TAT	GGG	TCC	AGC	TGT	GAG	TTC	TCC	TGT	GAG	CAG	GGT	TTT
ser	ala	ser	gly	ser	phe	arg	tyr	gly	ser	ser	cys	glu	phe	ser	cys	glu	gln	gly	phe
GTG	TTG	AAG	GGA	TCC	AAA	AGG	CTC	CAA	TGT	GGC	CCC	ACA	GGG	GAG	TGG	GAC	AAC	GAG	AAG
val	leu	lys	gly	ser	lys	arg	leu	gln	cys	gly	pro	thr	gly	glu	trp	asp	asn	glu	lys
CCC	ACA	TGT	GAA	GCT	GTG	AGA	TGC	GAT	GCT	GTC	CAC	CAG	CCC	CCG	AAG	GGT	TTG	GTG	AGG
pro	thr	cys	glu	ala	val	arg	cys	asp	ala	val	his	gln	pro	pro	lys	gly	leu	val	arg
TGT	GCT	CAT	TCC	CCT	ATT	GGA	GAA	TTC	ACC	TAC	AAG	TCC	TCT	TGT	GCC	TTC	AGC	TGT	GAG
cys	ala	his	ser	pro	ile	gly	glu	phe	thr	tyr	lys	ser	ser	cys	ala	phe	ser	cys	glu
GAG	GGA	TTT	GAA	TTA	TAT	GGA	TCA	ACT	CAA	CTT	GAG	TGC	ACA	TCT	CAG	GGA	CAA	TGG	ACA
glu	gly	phe	glu	leu	tyr	gly	ser	thr	gln	leu	glu	cys	thr	ser	gln	gly	gln	trp	thr
GAA	GAG	GTT	CCT	TCC	TGC	CAA	GTG	GTA	AAA	TGT	TCA	AGC	CTG	GCA	GTT	CCG	GGA	AAG	ATC
glu	glu	val	pro	ser	cys	gln	val	val	lys	cys	ser	ser	leu	ala	val	pro	gly	lys	ile
AAC	ATG	AGC	TGC	AGT	GGG	GAG	CCC	GTG	TTT	GGC	ACT	GTG	TGC	AAG	TTC	GCC	TGT	CCT	GAA
asn	met	ser	cys	ser	gly	glu	pro	val	phe	gly	thr	val	cys	lys	phe	ala	cys	pro	glu
GGA	TGG	ACG	CTC	AAT	GGC	TCT	GCA	GCT	CGG	ACA	TGT	GGA	GCC	ACA	GGA	CAC	TGG	TCT	GGC
gly	trp	thr	leu	asn	gly	ser	ala	ala	arg	thr	cys	gly	ala	thr	gly	his	trp	ser	gly
CTG	CTA	CCT	ACC	TGT	GAA	GCT	CCC	ACT	GAG	TCC	AAC	ATT	CCC	TTG	GTA	GCT	GGA	CTT	TCT
leu	leu	pro	thr	cys	glu	ala	pro	thr	glu	ser	asn	ile	pro	leu	val	ala	gly	leu	ser
GCT	GCT	GGA	CTC	TCC	CTC	CTG	ACA	TTA	GCA	CCA	TTT	CTC	CTC	TGG	CTT	CGG	AAA	TGC	TTA
ala	ala	gly	leu	ser	leu	leu	thr	leu	ala	pro	phe	leu	leu	trp	leu	arg	lys	cys	leu
CGG	AAA	GCA	AAG	AAA	TTT	GTT	CCT	GCC	AGC	AGC	TGC	CAA	AGC	CTT	GAA	TCA	GAC	GGA	AGC
arg	lys	ala	lys	lys	phe	val	pro	ala	ser	ser	cys	gln	ser	leu	glu	ser	asp	gly	ser

FIG. 2C

TAC CAA AAG CCT TCT TAC ATC CTT TAA GTTCAAA AGAATCAGAA ACAGGTGCAT CTGGGGAACT A
tyr gln lys pro ser tyr ile leu ***
GAGGGATAC ACTGAAGTTA ACAGAGACAG ATAACCTCTCC TCGGGTCTCT GGCCTTCTT GCCTACTATG CCAG
ATGCCCT TTATGGCTGA AACCGCAACA CCCATCACCA CTTCAATAGA TCAAAGTCCA GCAGGCAAGG ACGGCCCT
TCA ACTGAAAAGA CTCAGTGTTT CCTTTCCTAC TCTCAGGATC AAGAAAGTGT TGGCTAATGA AGGGAAGGA
TATTTTCTTC CAAGCAAAGG TGAAGAGACC AAGACTCTGA AATCTCAGAA TTCCTTTTCT AACTCTCCCT TG
CTGGCTGT AAAATCTTGG CACAGAAACA CAATATTTTG TGGCTTCTT TCTTTTGCCC TTCACAGTGT TTCGA
CAGCT GATTACACAG TTGCTGTCTAT AAGAATGAAT AATAATTATC CAGAGTTTAG AGGAAAAAA TGACTAAA
AA TATTATAACT TAAAAAATG ACAGATGTTG AATGCCACCA GGCAATGCA TGGAGGGTTG TTAATGGTGC
AATCCCTACT GAAATGCTCTG TCGGAGGGTT ACTATGCACA ATTAAATCAC TTTCATCCCT ATGGGATTCA GTG
CTTCTTA AAGAGTTCTT AAGGATTGTG ATATTTTAC TTGCATTGAA TATATTATAA TCTTCCATAC TTCCTC
ATTG AATACAAGTG TGGTAGGGAC TTAATAAACT TGTAATGCT GTCAACTATG ATATGGTAAA AGTTACTTA
T TCTAGATTAC CCCCTCATTG TTTATTAAACA AATTATGTTA CATCTGTTT AAATTIATTT CAAAAAGGGA A
ACTATTGTC CCTAGCAAG GCATGATGTT AACCAGAATA AAGTCTCGAG TGTTTTACT ACAGTTGTTT TTTC
AAAACA TGGTAGAATT GGAGAGTAAA AACTGAATGG AAGGTTTGT TATTGTCAGA TATTTTTC GAAATAT
GTG GTTCCACGA TGAATAACTT CCATGAGGCC AAACGTTTGG AACTAATAAA AGCATAAATG CAAACACACA
AAGGTATAAT TTTATGAATG TCTTTGTTGG AAAAGAATAC AGAAAGATGG ATGTGCTTG CATTCCTACA AA
GATGTTG TCAGATGTGA TATGTAAACA TAATCTTGT ATATTATGGA AGATTTTAAA TTCACAATAG AAAT

FIG. 2D

CACCA TGTAAGAAGAG TCATCTGGTA GATTTTAAAC GAATGAAGAT GTCTAATAGT TATTCCTCTAT TTGTTTTC
TT CTGTATGTTA GGGTGCTCTG GAAGAGAGGA ATGCCTGTGT GAGCAAGCAT TTATGTTTAT TTATAAGCAG
ATTAAACAAT TCCAAAGGAA TCTCCAGTTT TCAGTTGATC ACTGGCAATG AAAAATTCTC AGTCAGTAAT TGC
CAAAGCT GCTCTAGCCT TGAGGAGTGT GAGAAATCAAA ACTCTCCTAC ACTTCCATTA ACTTAGCATG TGTGTA
AAAA AAAAGTTTCA GAGAAGTTCT GGCTGAACAC TGGCAACGAC AAAGCCAACA GTCAAAACAG AGATGTGAT
A AGGATCAGAA CAGCAGAGGT TCTTTTAAAG GGCAGAAAA ACTCTGGGAA ATAAGAGAGA ACAACTACTG T
GATCAGGCT ATGTATGGAA TACAGTGTTA TTTTCTTTGA AATTGTTAA GTGTGTAAA TATTTATGTA AACT
GCATTA GAAATTAGCT GTGTGAAATA CCAGTGCGT TTGTGTTTGA GTTTTATTGA GAATTTTAAA TTATAAC
TTA AAATATTTTA TAATTTTAA AGTATATATT TATTTAAGCT TATGTCAGAC CTATTGACA TAACACTATA
AAGGTTGACA ATAAATGTGC TTATGTTT

FIG. 2E

FIG. 3A

CGGGCCCTCAC TGGCTTCAGG AGCTGAATAC CCTCCAGGC ACACACAGGT GGGACACAAA TAAGGGTTTT GGA
 ACCACTA TTTTCTCATC ACGACAGCAA CTTAAA ATG CCT GGG AAG ATG GTC GTG ATC CTT GGA GCC
 met pro gly lys met val val ile leu gly ala
 TCA AAT ATA CTT TGG ATA ATG TTT GCA GCT TCT CAA GCT TTT AAA ATC GAG ACC ACC CCA
 ser asn ile leu trp ile met phe ala ala ser gln ala phe lys ile glu thr thr pro
 GAA TCT AGA TAT CTT GCT CAG ATT GGT GAC TCC GTC TCA TTG ACT TGC AGC ACC ACA GGC
 glu ser arg tyr leu ala gln ile gly asp ser val ser leu thr cys ser thr thr gly
 TGT GAG TCC CCA TTT TTC TCT TGG AGA ACC CAG ATA GAT AGT CCA CTG AAT GGG AAG GTG
 cys glu ser pro phe phe ser trp arg thr gln ile asp ser pro leu asn gly lys val
 ACG AAT GAG GGG ACC ACA TCT TCT GGT GAA ACC CAG ATA GAT AGT CCA CTG AAT GGG AAG GAA CAC
 thr asn glu gly thr thr ser thr leu thr met asn pro val ser phe gly asn glu his
 TCT TAC CTG TGC ACA GCA ACT TGT GAA TCT AGG AAA TTG GAA AAA GGA ATC CAG GTG GAG
 ser tyr leu cys thr ala thr cys glu ser arg lys leu glu lys gly ile gln val glu
 ATC TAC TCT TTT CCT AAG GAT CCA GAG ATT CAT TTG AGT GGC CCT CTG GAG GCT GGG AAG
 ile tyr ser phe pro lys asp pro glu ile his leu ser gly pro leu glu ala gly lys
 CCG ATC ACA GTC AAG TGT TCA GTT GCT GAT GTA TAC CCA TTT GAC AGG CTG GAG ATA GAC
 pro ile thr val lys cys ser val ala asp val tyr pro phe asp arg leu glu ile asp
 TTA CTG AAA GGA GAT CAT CTC ATG AAG AGT CAG GAA TTT CTG GAG GAT CCA GAC AGG AAG
 leu leu lys gly asp his leu met lys ser gln glu phe leu glu asp ala asp arg lys
 TCC CTG GAA ACC AAG AGT TTG GAA GTA ACC TTT ACT CCT GTC ATT GAG GAT ATT GGA AAA
 ser leu glu thr lys ser leu glu val thr phe thr pro val ile glu asp ile gly lys
 GTT CTT GTT TGC CGA GCT AAA TTA CAC ATT GAT GAA ATG GAT TCT GTG CCC ACA GTA AGG
 val leu val cys arg ala lys leu his ile asp glu met asp ser val pro thr val arg

CAG GCT GTA AAA GAA TTG CAA GTC TAC ATA TCA CCC AAG AAT ACA GTT ATT TCT GTG AAT
 gln ala val lys glu glu leu gln val tyr ile ser pro lys asn thr val ile ser val asn

 CCA TCC ACA AAG CTG CAA GAA GGT GGC TCT GTG ACC ATG ACC TGT TCC AGC GAG GGT CTA
 pro ser thr lys leu gln glu gly gly ser val thr met thr cys ser ser glu gly leu

 CCA GCT CCA GAG ATT TTC TGG AGT AAG AAA TTA GAT AAT GGG AAT CTA CAG CAC CTT TCT
 pro ala pro glu ile phe trp ser lys lys leu asp asn gly asn leu gln his leu ser

 GGA AAT GCA ACT CTC ACC TTA ATT GCT ATG AGG ATG GAA GAT TCT GGA ATT TAT GTG TGT
 gly asn ala thr leu thr leu ile ala met arg met glu asp ser gly ile tyr val cys

 GAA GGA GTT AAT TTG ATT GGG AAA AAC AGA AAA GAG GTG GAA TTA ATT GTT CAA GCA TTC
 glu gly val asn leu ile gly lys asn arg lys glu val glu leu ile val gln ala phe

 CCT AGA GAT CCA GAA ATC GAG ATG AGT GGT GGC CTC GTG AAT GGG AGC TCT GTC ACT GTA
 pro arg asp pro glu ile glu met ser gly gly leu val asn gly ser ser val thr val

 AGC TGC AAG GTT CCT AGC GTG TAC CCC CTT GAC CGG CTG GAG ATT GAA TTA CTT AAG GGG
 ser cys lys val pro ser val tyr pro leu asp arg leu glu ile glu leu leu lys gly

 GAG ACT ATT CTG GAG AAT ATA GAG TTT TTG GAG GAT ACG GAT ATG AAA TCT CTA GAG AAC
 glu thr ile leu glu asn ile glu phe phe leu glu asp thr asp met lys ser leu glu asn

 AAA AGT TTG GAA ATG ACC TTC ATC CCT ACC ATT GAA GAT ACT GGA AAA AGG CAG AGT ACG CAA
 lys ser leu glu met thr phe phe phe leu glu asp thr val leu val lys ala leu val cys

 CAG GCT AAG TTA CAT ATT GAT GAC ATG GAA TTC GAA CCC AAA CAA AGG CAG AGT ACG CAA
 gln ala lys leu his ile asp asp met glu phe phe glu pro lys gln arg gln ser thr gln

 ACA CTT TAT GTC AAT GTT GCC CCC AGA GAT ACA ACC GTC TTG GTC AGC CCT TCC TCC ATC
 thr leu tyr val asn val ala pro arg asp thr thr val leu val ser pro ser ser ile

 CTG GAG GAA GGC AGT TCT GTG AAT ATG ACA TGC TTG ACC CAG GGC TTT CCT GCT CCG AAA
 leu glu glu gly ser ser val asn met thr cys leu ser gln gly phe pro ala pro lys

FIG. 3B

ATC/CTG TGG AGC AGG CAG CTC CCT AAC GGG GAG CTA CAG CCT CTT TCT GAG AAT GCA ACT
 ile leu trp ser arg gln leu pro asn gly glu leu gln pro leu ser glu asn ala thr
 CTC ACC TTA ATT TCT ACA AAA ATG GAA GAT TCT GGG GTT TAT TTA TGT GAA GGA ATT AAC
 leu thr leu ile ser thr lys met glu asp ser gly val tyr leu cys glu gly ile asn
 CAG GCT GGA AGA AGC AGC AGA AAG GAA CTG GAA TTA ATT ATC CAA GTT ACT CCA AAA GAC ATA
 gln ala gly arg ser arg lys lys glu val glu leu ile ile gln val thr pro lys asp ile
 AAA CTT ACA GCT TTT CCT TCT GAG AGT GTC AAA GAA GGA GAC ACT GTC ATC TCT TGT
 lys leu thr ala phe pro pro ser glu ser val lys glu gly asp thr val ile ser cys
 ACA TGT GGA AAT GTT CCA GAA ACA TCG ATA ATC CTG AAG AAA AAA GCG GAG ACA GGA GAC
 thr cys gly asn val pro glu thr trp ile ile leu lys lys ala glu thr gly asp
 ACA GTA CTA AAA TCT ATA GAT GGC GCC TAT ACC ATC CGA AAG GCC CAG TTG AAG GAT GCG
 thr val leu lys ser ile asp gly ala tyr thr ile arg lys ala gln leu lys asp ala
 GGA GTA TAT GAA TGT GAA TCT AAA AAC AAA GGT GGC TCA CAA TTA AGA AGT TTA ACA CTT
 gly val tyr glu cys glu ser lys asn lys val gly ser gln leu arg ser leu thr leu
 GAT GTT CAA GGA AGA GAA AAC AAC AAA GAC TAT TTT TCT CCT GAG CTT CTC GTG CTC TAT
 asp val gln gly arg glu asn asn lys asp tyr phe ser pro glu leu val leu tyr
 TTT GCA TCC TCC TTA ATA ATA CCT GCC ATT GGA ATG ATA ATT TAC TTT GCA AGA AAA GCC
 phe ala ser ser leu ile ile pro ala ile gly met ile ile tyr phe ala arg lys ala
 AAC ATG AAG GGG TCA TAT AGT CTT GTA GAA GCA CAG AAA TCA AAA GTG TAG CTAATGCTTG
 asn met lys gly ser tyr ser leu val glu ala gln lys ser lys val ***
 ATATGTTCAA CTGGAGACAC TATTTATCTG TGCAAATCCT TGATACTGCT CATCATTCCT TGAGAAAAAC AAT
 GAGCTGA GAGGCAGACT TCCCTGAATG TATTGAACTT GGAAGAAAT GCCCATCTAT GTCCCTTGCT GTGAGC
 AAGA AGTCAAAGTA AACTTGCTG CCTGAAGAAC AGTAACTGCC ATCAAGATGA GAGAACTGGA GGAGTTCCT
 T GATCTGTATA TACAATAACA TAATTGTAC ATATGTAAAA TAAAATTATG CCATAGCAAG ATTGCTTAAAA

FIG. 3C

TAGCAACAC TCTATATTTA GATTGTTAAA ATAACTAGTG TTGCTTGGAC TATTATAATT TAATGCATGT TAGG
AAAAAT TCACATTAAAT ATTTGCTGAC AGCTGACCCTT TGTCACTCTTT CTTCATATTT ATTCCCTTTC ACAAAT
TTT ATTCCCTATAT AGTTTATTGA CAATAATTTC AGTTTGTGA AAGATGCCGG GTTTTATATT TTTATAGACA
AATAATAAGC AAAGGGAGCA CTGGGTTGAC TTTCAGGTAC TAAATACCCTC AACCTATGGT ATAATGGTTG AC
TGGGTTTC TCTGTATAGT ACTGGCATGG TACGGAGATG TTTCACGAAG TTTGTTTCATC AGACTCCTGT GCAAC
TTTCC CAATGTGGCC TAAAAATGCA ACTTCTTTTT ATTTCTTTT GTAAATGTTT AGGTTTTTT GTATAGTA
AA GTGATAATTT CTGGAATTAA AAA

FIG. 3D

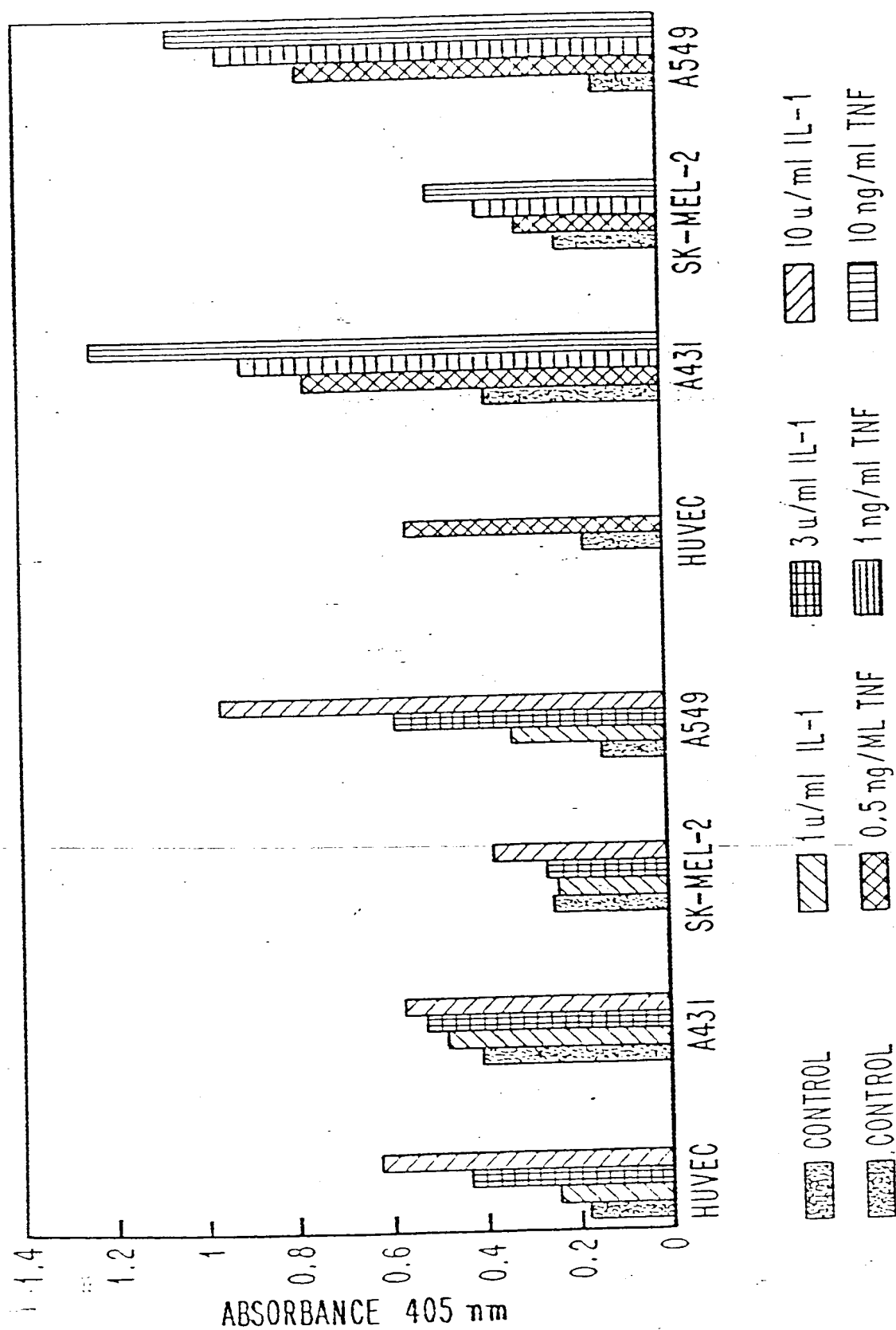


FIG. 4

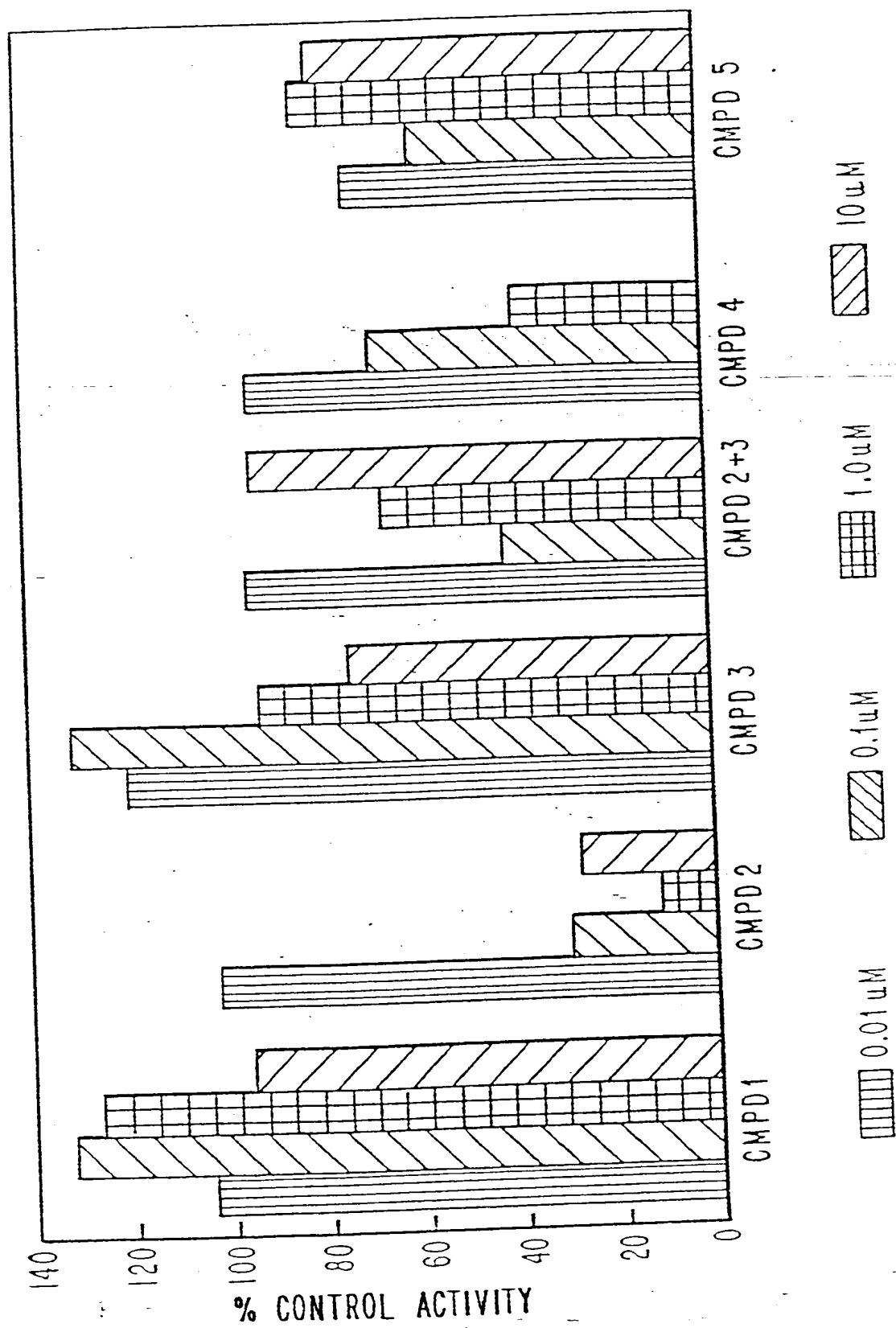


FIG. 5

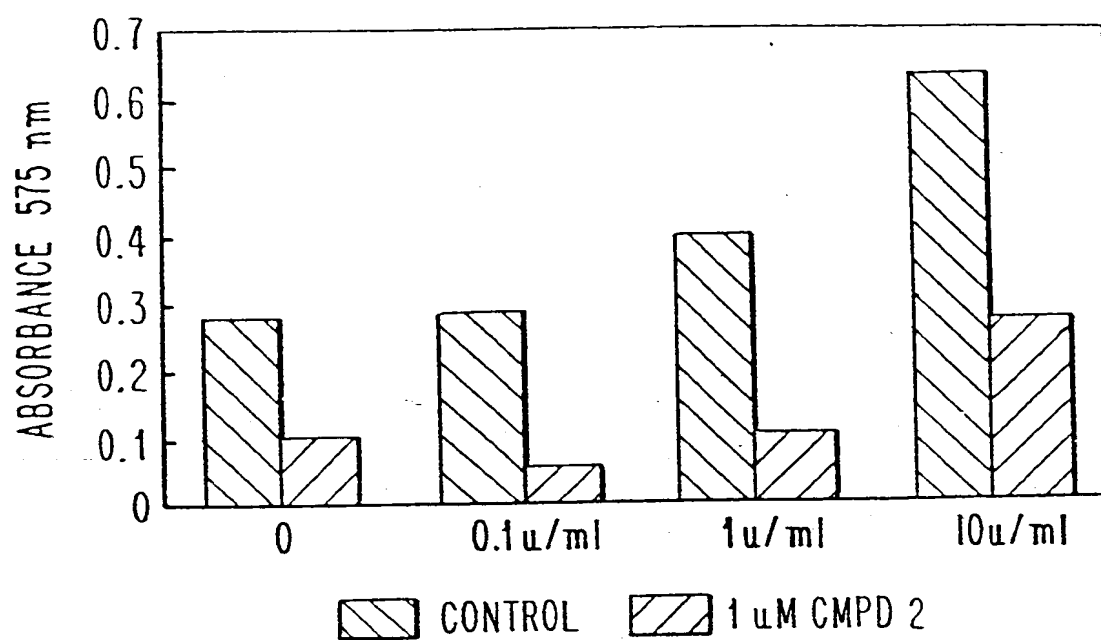


FIG. 6A

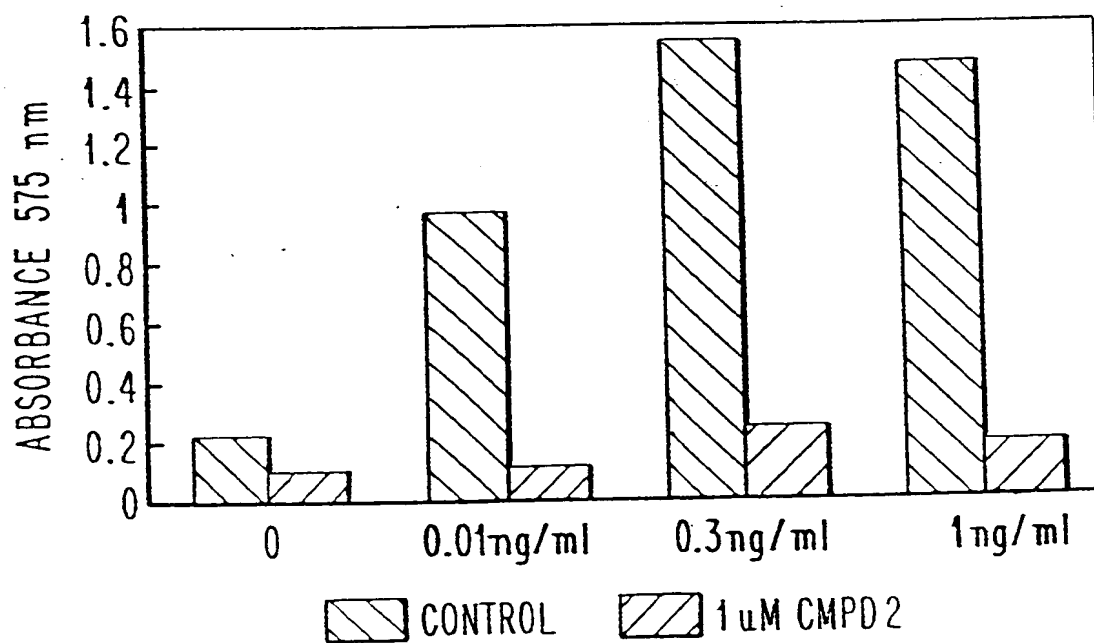


FIG. 6B

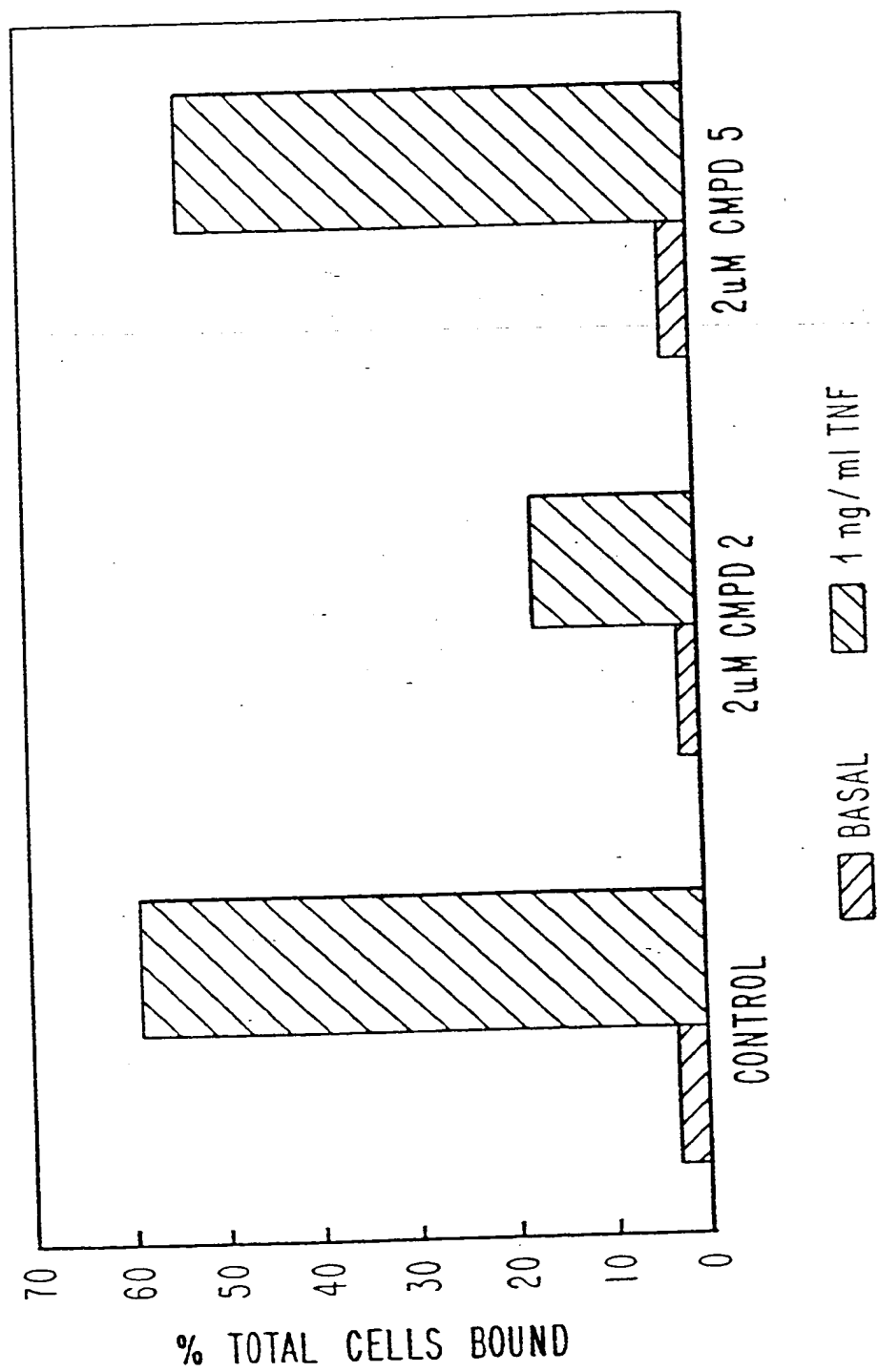
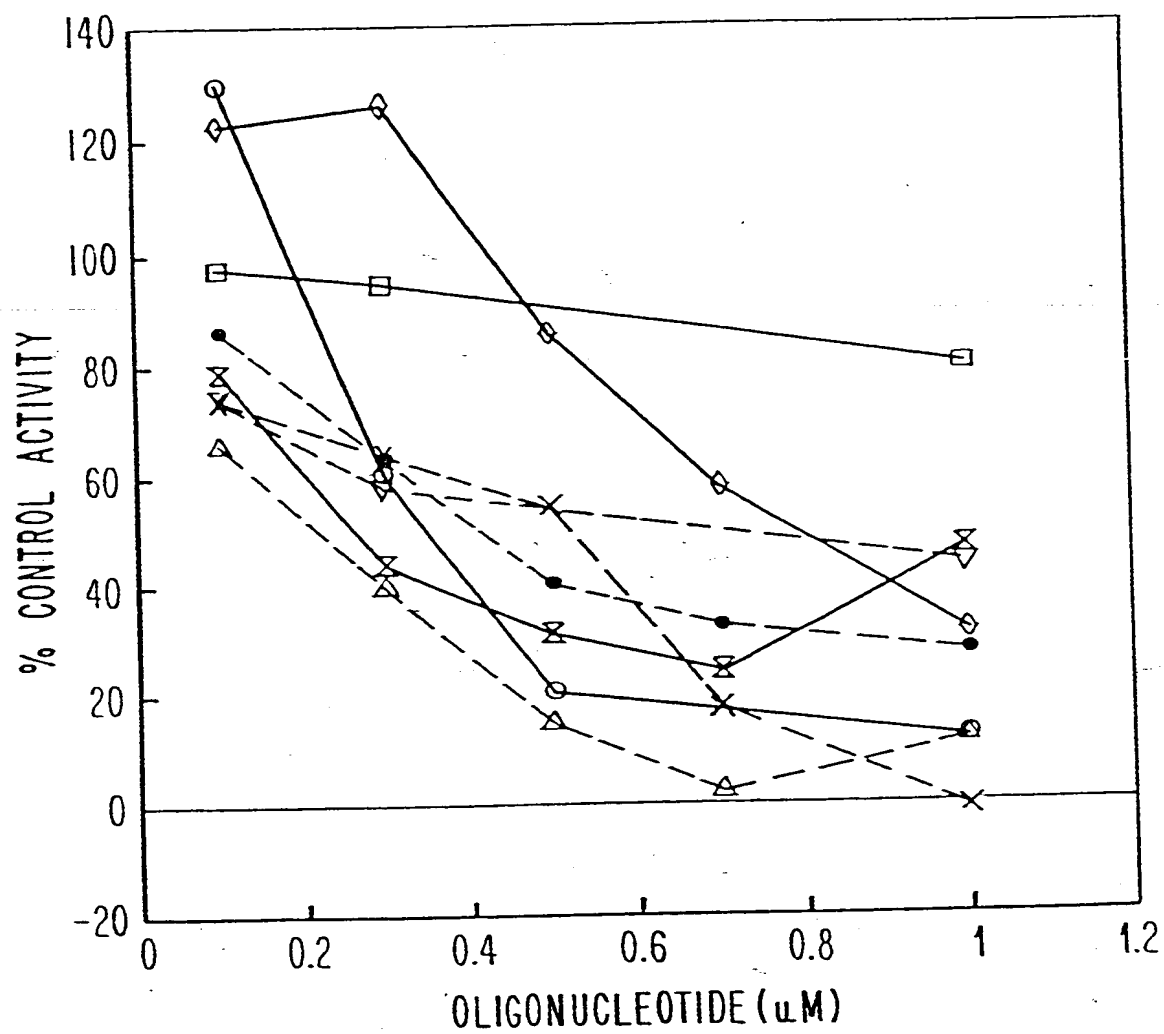


FIG. 7



• 1570

○ 3067

▽ 1931

□ 1932

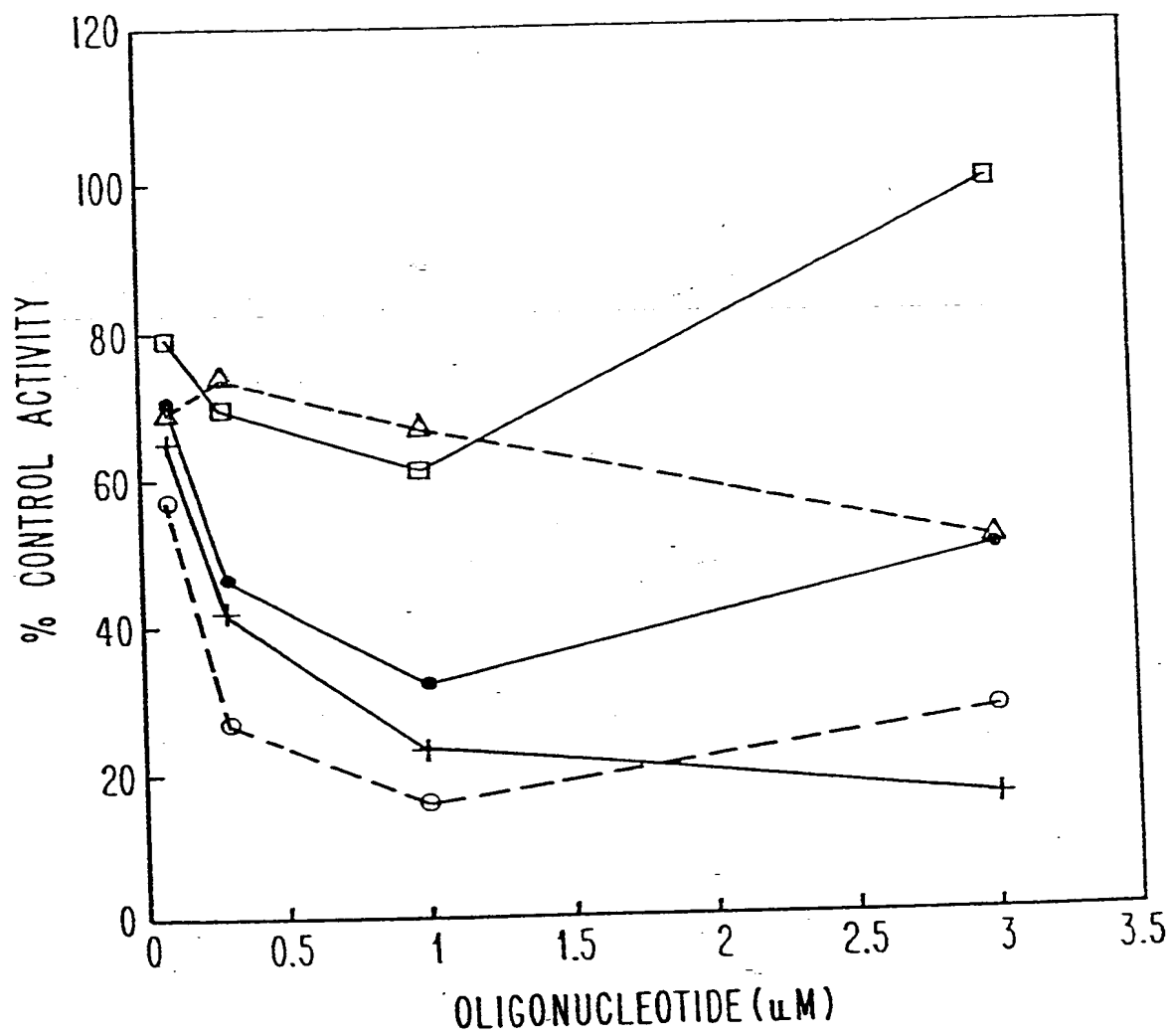
× 1939

◇ 2307

△ 2302

⊗ 1938

FIG. 8



• 1570

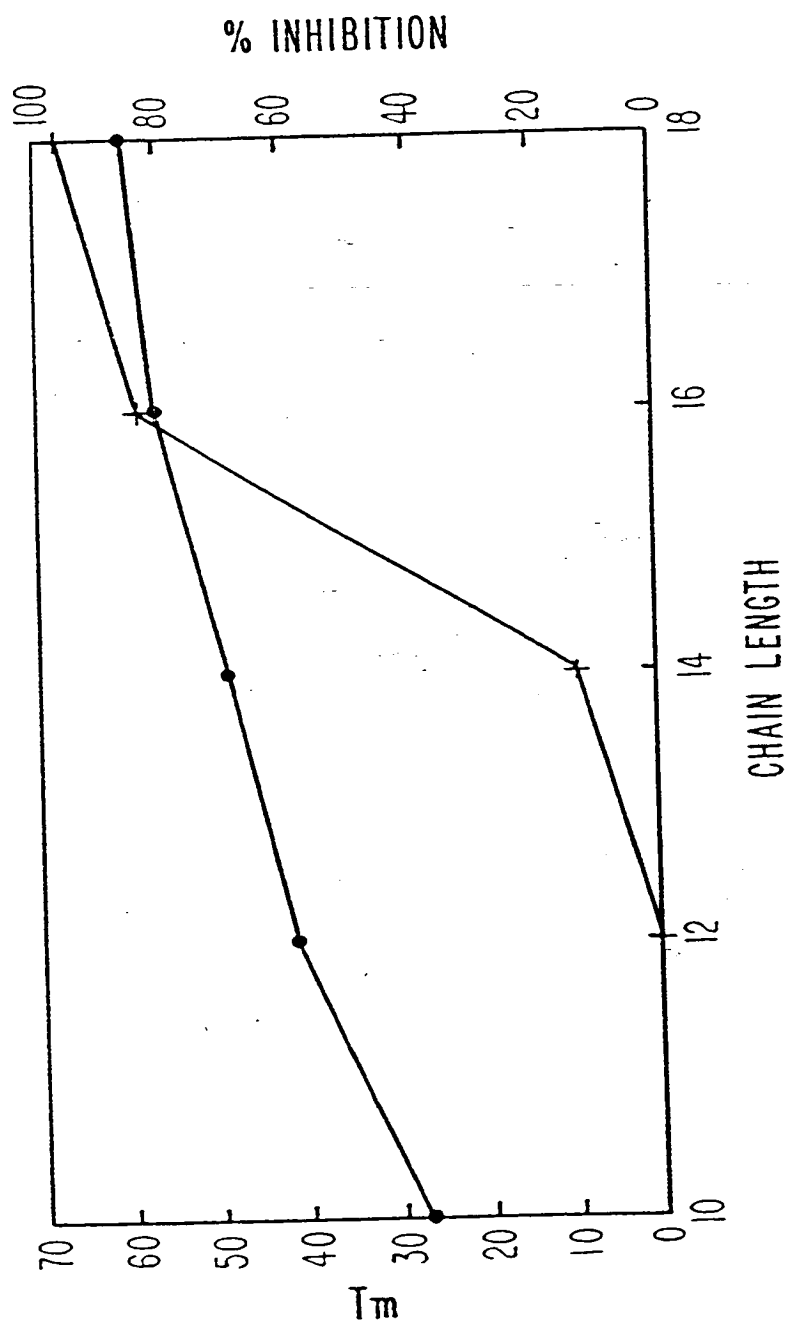
+ 1939

Δ 1940

\square 1821

\circ 2302

FIG. 9



• T_m + % INHIBITION
100 nM OLIGONUCLEOTIDE

FIG. 10

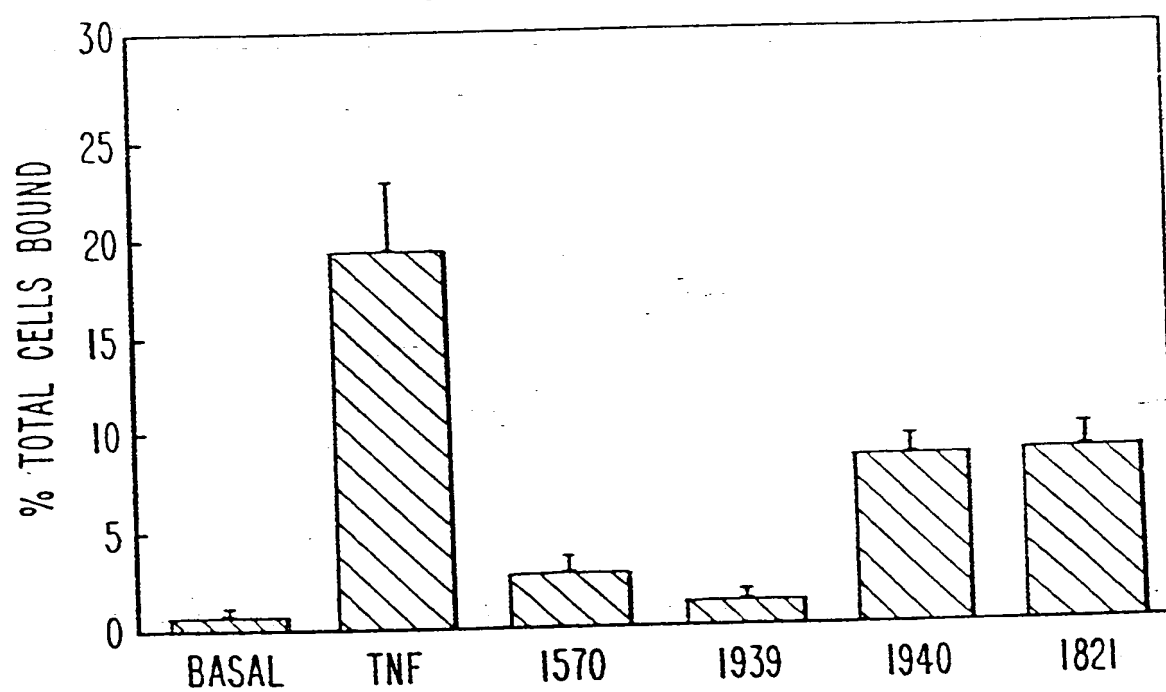


FIG. 11

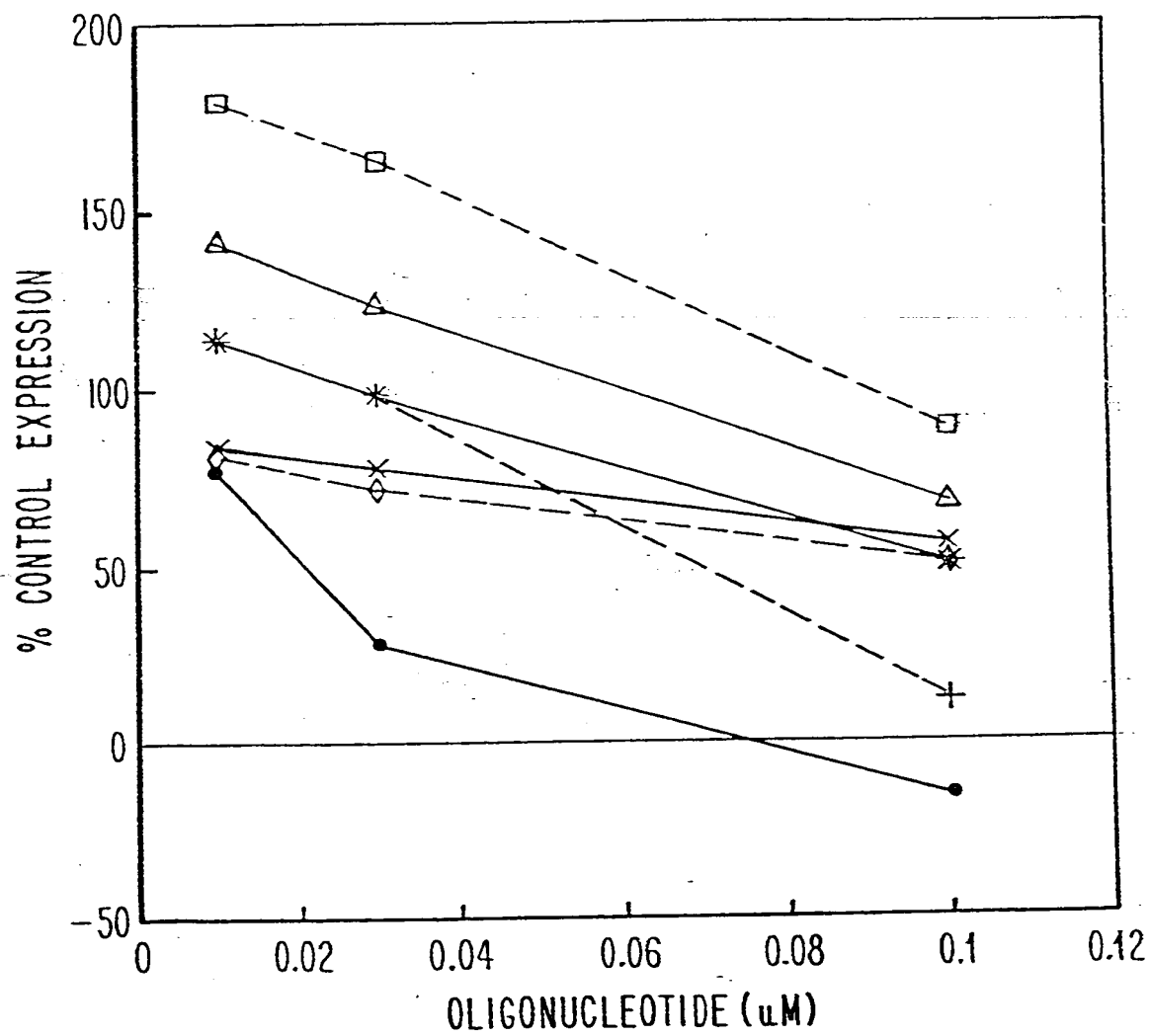


FIG. 12

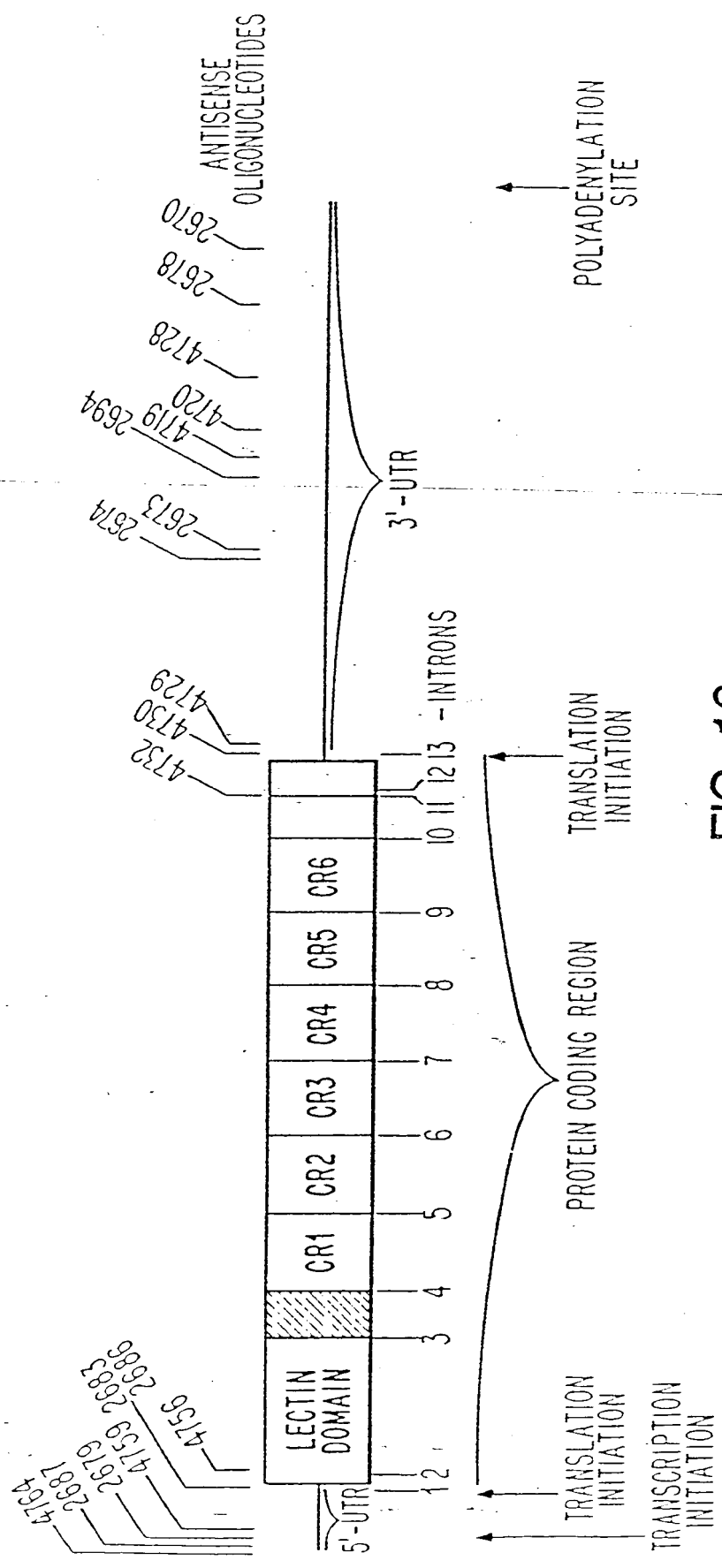


FIG. 13

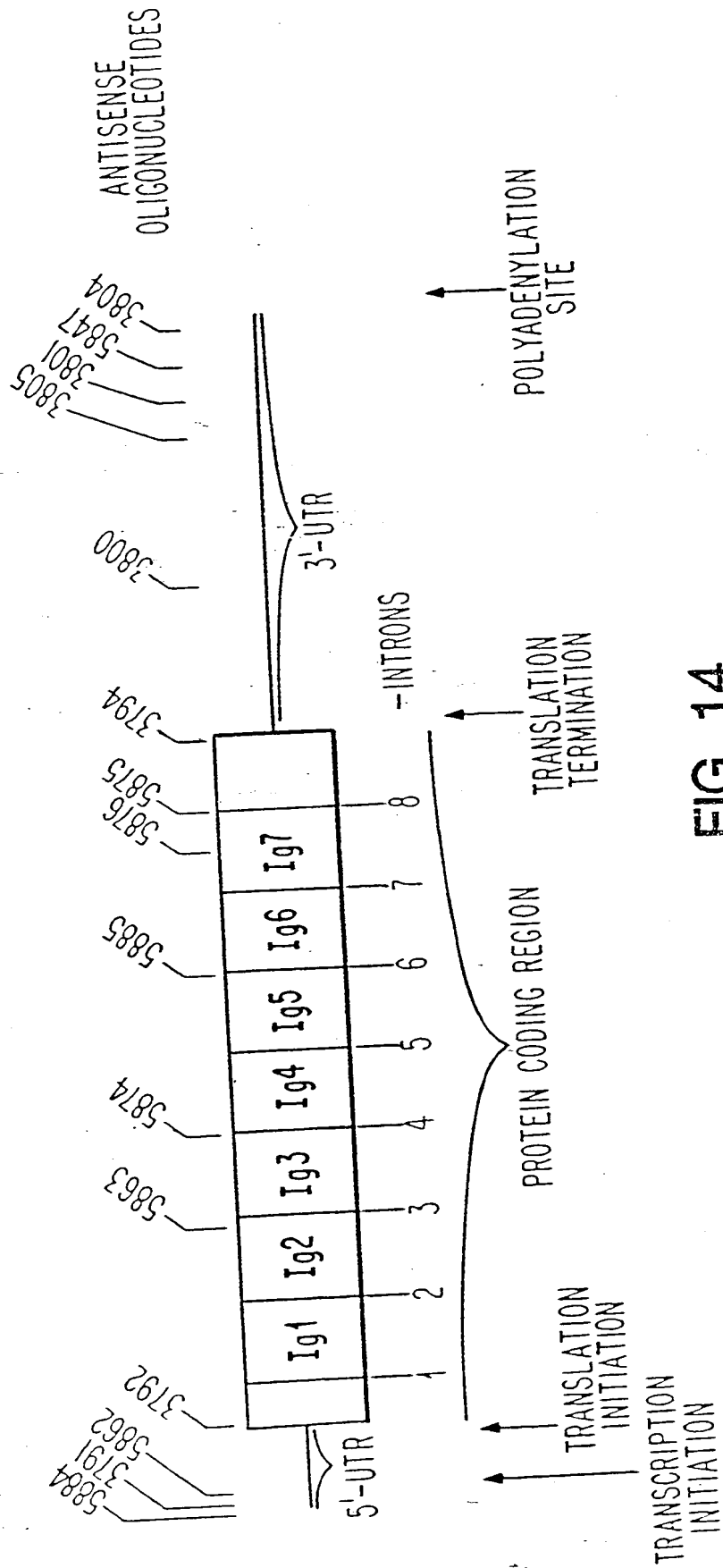


FIG. 14

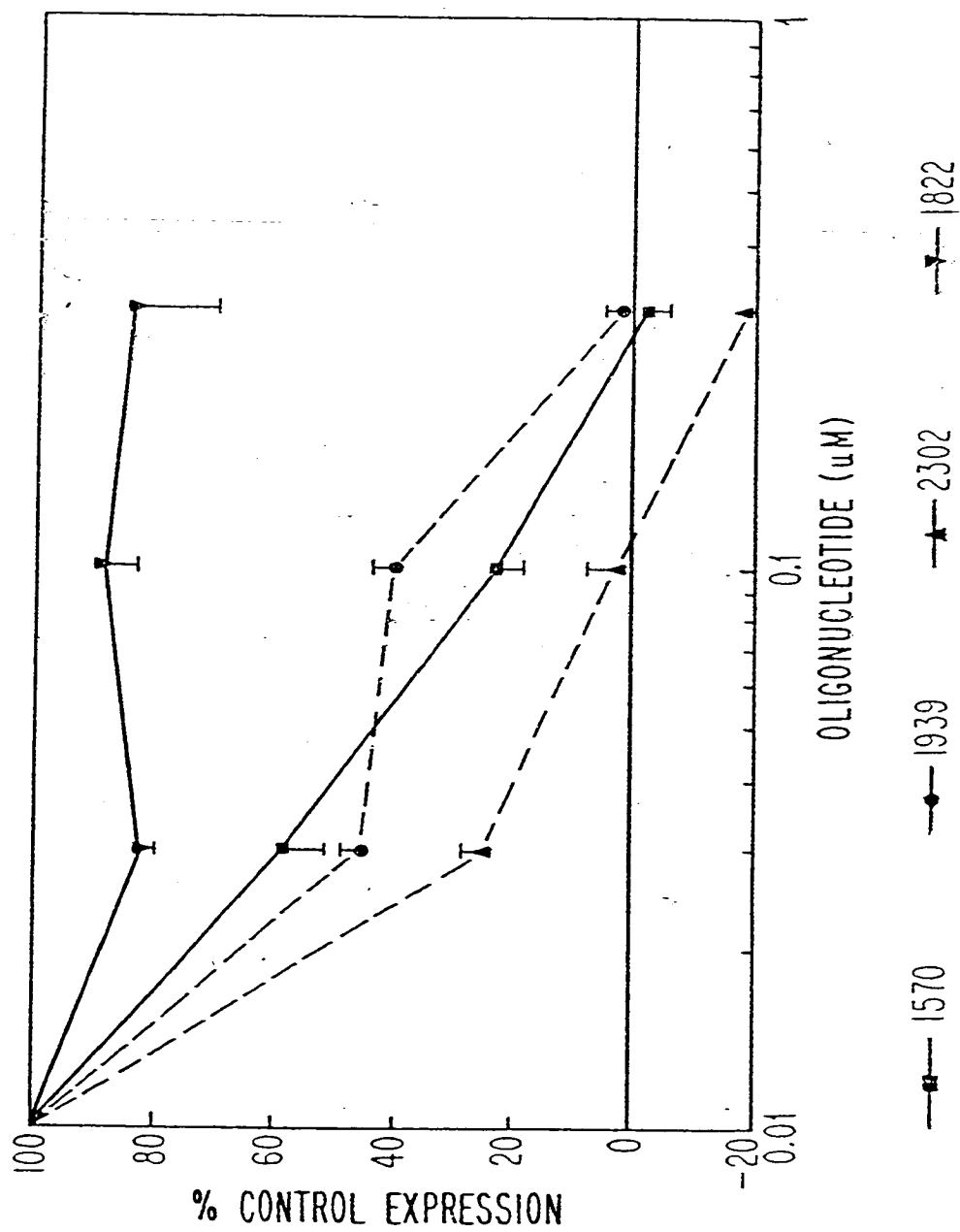


FIG. 15

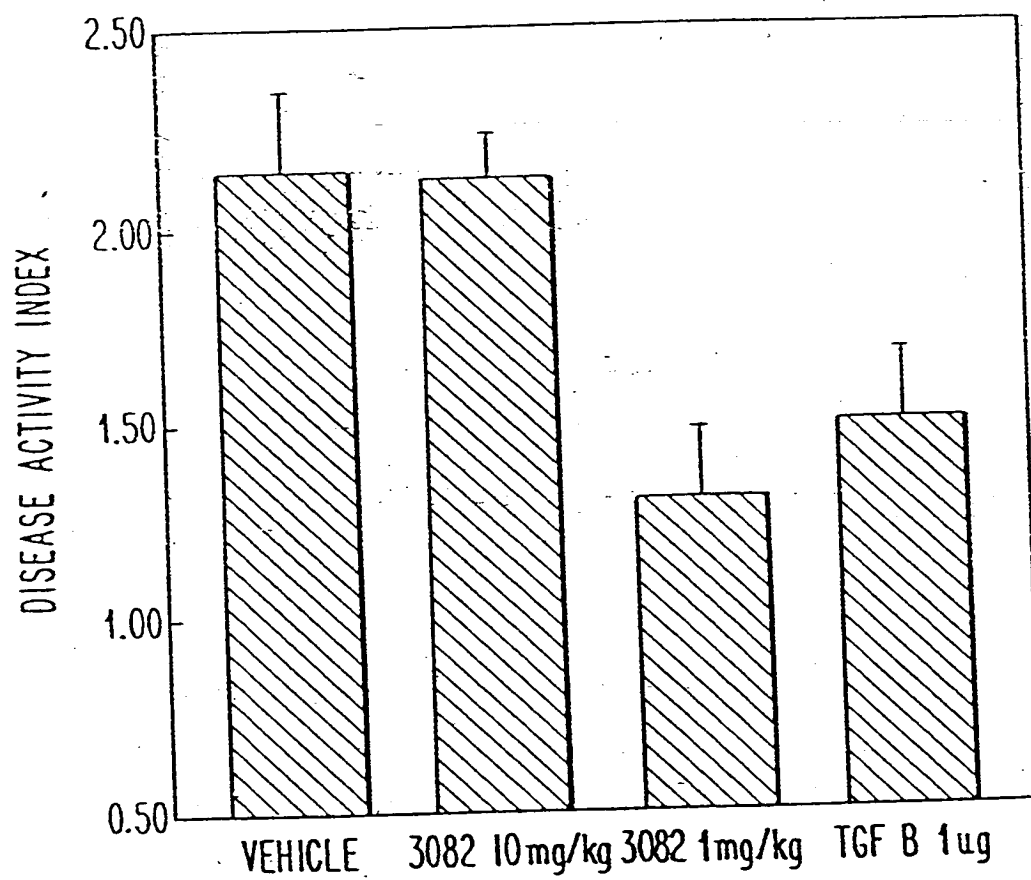


FIG. 16